Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT
Staff Report on Current Scientific Studies Supported by the Federal Government

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DR. WAGNER: Let me invite Michelle Groman and Jeremy Sugarman to the table. This next session will be around our commission receiving a staff report. Michelle Groman is senior policy and research analyst for our commission, and has served as a lead staffer on this project. But we are going to hear first from Jeremy.

Jeremy Sugarman is going to report to us about the empirical project, as we have been calling it, that the staff has been conducting to collect data from government agencies that support research involving

human subjects. It's an important part of our information-gathering process for the human subjects protection review, because it's with this information that we will -- with some certainty, we hope -- be able to describe to the President the universe of human subjects research supported by the Federal Government that is being done domestically and internationally.

Jeremy is the Harvey Meyerhoff professor of bioethics and medicine, professor of medicine, and professor of health policy and management, and deputy director of medicine at the Berman Institute of Bioethics at Johns Hopkins University, internationally recognized leader in the field of biomedical ethics, and with particular expertise in the application of empirical methods and evidence-based standards, for the evaluation and analysis of bioethical issues.

His contributions to both medical ethics and policy include his work on ethics of informed consent, tissue banking, stem cell research, international HIV prevention research, and research oversight. He has served with -- as a senior policy advisor and research analyst for the White House Advisory Committee on Human

Radiation Experiments, and a consultant to the National Bioethics Advisory Commission, was a founding director of the Trent Center for Bioethics, Humanities, and History of Medicine at Duke, where he was also a professor of medicine and philosophy. He is a faculty affiliate of the Kentucky Institute of Ethics at Georgetown University.

We are pleased to have him here to use up all his spare time with the commission. Jeremy, the floor is yours.

DR. SUGARMAN: Thanks, Jim, for the long introduction. It's helped the search for my slides.

(Laughter.)

DR. SUGARMAN: Thank you. While the slides are being located, I appreciate the opportunity to be able to share with you some of the work that we have been doing to provide some data to help inform the committee's deliberations.

And much of the day-to-day legwork on this project goes to Michelle Groman who, without her amazing energy and attention to detail, none of this work would have been possible. So Michelle is doing

the day-to-day work of actually finding the presentation. But, really, without Michelle's efforts, we wouldn't have anything to really share with you. That said, I am going to talk, and Michelle is going to be there with all the details.

So, going back to the President's charge to the group, we have heard this letter before, but I just want to call out this one sentence, because this is where we take as our jumping off point. "To conduct a thorough review of human subjects protection to determine if federal regulations and international standards adequately guard the health and well-being of participants in scientific studies supported by the Federal Government." A sentence, an important sentence, that raises a couple of issues.

First of all, there are no systematic data available across federal agencies about the scientific studies supported by the Federal Government. Without that sort of data, without that information, it's hard to know what recommendations will be done. What's the purpose of the committee's deliberation? How will you know you're getting it right?

We know that the research ethics landscape and the popular press brings to light bad cases. We don't hear about good cases. We don't know what types of research is being done, where it's being done, and what the federal investment would do.

There is also limited available systematic information about this very central question about how well the regulations and standards guard the health and well-being of participants, the second clause in the President's charge. And that, in part, is an empirical question, as well as it is a conceptual question.

The thought going forward in conversations with the commission and the staff is that such data are needed to help inform deliberations, and that's where this presentation will focus.

The commission decided, early on, to initiate a landscape project, which I will discuss in more detail, to provide basic information that is not available everywhere. You have heard multiple speakers provide testimony in that regard -- Zeke Emanuel among them this morning -- saying we don't have information about what the landscape looks like for research

sponsors. And so the commission has decided to move forward, and I will give you an update on that project.

To meet this second clause of that charge, we offer up a series of potential projects that may or may not be appropriate to help inform that second part, about how well protections are working.

In order to help inform our work, we assembled an empirical advisory group to help provide expertise to help guide what particular kinds of questions would we ask in the landscape project, and also to propose and evaluate other empirical projects that can inform the commission's response. The goal here is to provide that expertise and to sort of add the facts, so that you can have the value debate.

The empirical advisory group is a fantastic group of individuals that actually came together to work on this. Christine and Dan, as commissioners, joined us. Rob Califf, from Duke, who has conducted multinational trials, who gave testimony in an earlier meeting. Ruth Faden at Johns Hopkins, who was the chair of the advisory committee on human radiation experiments. Ken Getz, an affiliate of Tufts who

provided -- who knows more about using larger databases, and other experts.

All right. So, the landscape project, as we set it out, was to define the landscape as we talked about it, and to provide these analyses.

Now, you will see there are 18 federal agencies here which are listed, which we had reason to believe were conducting scientific studies supported by the Federal Government. The agencies -- the time line for the project here was in March and June. We identified liaisons, and alerted them to the fact that the Presidential Commission was interested in these questions.

The data that we were going to ask for had to be clarified, and the tools were developed. So, because this has never been done, this is some basic work that the commission can claim as being critically important for knowing how you might map something like this. You had to create tools that would work across agencies, and then the agencies were asked to provide fiscal year 2010 data in August, and additional data to be due. The goal is to have all this information

available for your next meeting.

Now, this is now drilling down a bit. You can see on the top portion of this area the research project database. This is the Excel form that was sent to the agencies and asked them to fill out. Countless conversations with the help desk, with Michelle, to figure out exactly how these agencies could take very different information systems and provide this. We want to thank the agencies for doing this work.

So, what -- this kind of question seems simple, what we want to know, but it's a very difficult set of data to gather from the ways that agencies keep, in different ways, this information. And so, coming up with this approach has required lots of effort on the part of lots of agencies, and I won't name each of them here.

What that does -- quick study. In the research project database -- our very apt name for what we have, and what this is is the database that is being put together to drive the analyses. You can see here some of the data elements.

So, the current status is that all the

agencies contacted have responded. That's a start. Seventeen agencies have provided some or all project-level data for fiscal year 2010. So we haven't received all the information we need, but there have been good faith efforts upon the agencies to do so.

The Department of Defense has provided aggregate fiscal year 2010 and also the back year's data. But only aggregate data, feeling that the project-level data was something that they were not able to provide to us, with the way that they keep their information systems.

The empirical advisory group met, provided guidance, and we're in the process of finding a statistician who is properly trained to analyze the data. Potential analyses are to answer those basic landscape questions about the scientific studies, the institutions, and funding.

Now, the next steps are -- so we've now got a landscape. And the question is: What's next? And we are at a branch point here to decide which, if any, projects we would go forward with, depending on what would be useful to the commission.

One idea is to take this research project database which we have already assembled, and then compare it, if you will, to the clinicaltrials.gov database, which you have heard about. So what we know is that not all scientific studies supported by the Federal Government would be expected to be in clinicaltrials.gov. Those that would be related to drug and device-related research would be. But it leaves out the full range of studies. Now I can't tell you what that full range is until we do the analyses of the research project database. But we know in advance, going into this, that not all of it would be expected to be there.

So, what we could do by going and comparing what's in our, say, more comprehensive database to what's known in clinicaltrials.gov, would be for those studies where there is overlap, we will have almost participant-level information about those studies that are in our database which we don't currently have. We will also know whether there are studies that appear in our database that should have been listed in clinicaltrials.gov in the name of transparency which

aren't there.

And so, some type of analysis like this would require taking a picture of the clinicaltrials.gov database at a particular time, which is something that NLM is working on, in collaboration with Duke in a public-private partnership, to come up with a set database at a set point in time to be able to analyze those data.

A second possible step would be to review the abstracts that are not in clinicaltrials.gov. So clinicaltrials.gov gives us that rich information. But we don't have very detailed information about the science that is being done in the other settings. So this would require some type of selection of the abstracts, and to review them for the kinds of information of the subjects where it's located and the like, so that we can inform that.

This could be -- a sampling method could be used, or a comprehensive approach, but it would depend on what questions the commission wanted answered. One approach that has been suggested that we are exploring is a natural language analysis of the abstracts that

are there, so that instead of people going through and manually coding it, what you do is you take the full text and analyze the full text, and inductively come up with information that could inform our decisions. We don't know how feasible that is, but we're in the process of discussing with people who do natural language analysis. There is a recent publication that -- last week or this week in JAMA, for instance -- which is beginning to use these sort of methods in research.

The other empirical projects to consider -- now moving away from the research project database -- would be two possible projects that would provide more granularity to what's going on. One would be a web-based survey of investigators, and the other would be a systematic assessment of human subjects protections.

The advantages of conducting a web-based survey of investigators is we would get the perspective of one group of key stakeholders, not all. But they are people who are accustomed to answering web-based surveys. They may be very motivated, given the ANPRM,

to be part of this conversation, whereas normally they may resist, or not really enjoy doing another survey. And the potential domains, the advantage of going broader than the experiences of the commission or those who provide testimony is we might have more generalizable data about impressions, about what works, what doesn't, what kind of barriers are faced.

Could this ask questions, whether community engagement occurred, what's their experience with human subjects protection, what works and what doesn't, and whether they believe that important research projects have been delayed or abandoned because of procedural concerns. Did they not do something because they were concerned about the hoops and the bureaucracy that would be involved? Or what helped move things forward?

The final one is the systematic review. What we could do, unlike any other place, is once we have this research project database, is sample from the commission's database and do some type of stage-appropriate review which would mimic other projects that have been done in the past to do a centralized protocol review to see how well this

localized system actually is working, to interview key stakeholders, such as IRB chairs, investigators, perhaps research participants, community members, community advisory boards, and the like, and then conduct site visits.

Something like this is an enormous undertaking. But if the commission decided to take some type of review at some point and to pilot it, it might serve as a pilot for some kind of periodic program to say that a future commission, or a future group, or anyone wanting to look at this won't be left in the position of saying, "How well are the protections working," we will know how well the protections are working, and not be left to conjecture.

So, thank you for that overview, and I am happy to take questions.

DR. WAGNER: Thanks, Jeremy. Could we --

DR. GUTMANN: Thanks very much.

DR. WAGNER: Are you doing this one, or am I doing this one?

DR. GUTMANN: Go ahead.

(Laughter.)

DR. WAGNER: No, you're welcome to it, believe me.

DR. GUTMANN: No, no, no.

DR. WAGNER: Could we go back to that slide that had the domains on it? Is that easy to do, go back about two slides?

DR. SUGARMAN: Sure. I think.

DR. WAGNER: My understanding is when we initiated the empirical study that there was also this broader question around breadth and scope and volume, and how much is going on, what's involved, and, you know, what's the breadth of it, within which we could then ask these questions about community engagement and human subjects protection.

Are we going to get that out of this? Are we going to have a sense of -- that we've got some sort of a catalog that we can ask these quantitative questions about first, before the qualitative --

DR. SUGARMAN: So, currently, no. The kinds of questions we can answer are the ones delineated on the earlier slide that talked about what we can count. What's the nature of the research being conducted?

Which agencies? What's the investment? Where is the research being conducted? Without further linking, we are going to have less information about those issues.

What we could use the database for is the last project I mentioned, not necessarily the survey of investigators, would be to do a systematic sampling to begin to answer those questions. The concern about that is it's almost September, and the Commission is on track to report earlier than that.

DR. WAGNER: So we don't have key-word categories or something that we're going to sort these by?

DR. SUGARMAN: Correct.

DR. GUTMANN: So it seems to me -- and this is going to be a comment for you to react to -- it seems to me that we have to see first how good a database we can get. And until we can see that, there is -- we really have to see that.

And that means that let's see the extent to which we can get the agencies that are doing the research that -- for everything we know, and there is a lot of expertise around this table, we know quite a bit

about the kind of research that's been done historically and, you know, recently. We need to see what that database yields, and compare it to clinicaltrials.gov.

That is a really important -- to see where the overlap is and what we get that isn't in clinicaltrials.gov. And once we see that, and until we see that, I don't think we can make other judgments about where to go from there. That is my comment to get a reaction to. I just think, otherwise, we invest a lot of time and effort into empirical work that we have no idea at this point whether it's going to yield insights that we can use, as a commission, which is our job, as a bioethics commission, is to comment on the ethics.

So, I think we need -- we really need to see what the first empirical project -- the landscape project, which seems to me extremely worthwhile. And I would just urge, take this opportunity to urge, everybody in those agencies to cooperate fully with us, because if there is -- one thing that nobody we have spoken with disagrees with is the importance of this

level of transparency, where we're not revealing -- you know, we're not invading anybody's privacy. What we are being transparent about is what the government is funding.

DR. WAGNER: Yes, Christine?

DR. GRADY: I just wanted to mention that Jeremy pointed out the idea about the web-based survey of investigators, which was a proposal at the empirical advisory group that was in addition to but different than the landscape project. And the reason was because, to the extent that the commission is interested in things like community engagement and training, and the effect of the burdensomeness of rules and standards, that there were members of that group that felt like this was an opportunity in time to get investigators to respond to those kinds of issues and get data on that.

None of those questions are being asked in the landscape project, so those are pieces of data that we might be perhaps well-positioned to try to get in a systematic way. But it is a separate project, so I take your point very -- it is very important, so --

DR. WAGNER: Back to Amy's comment, Jeremy. Any response to that?

DR. SUGARMAN: So I think we have -- the first part is that analyzing the database we have is absolutely essential, and that we will know how the database is performing when we do the initial run of the fiscal year 2010 data about the research project database. So we will know what we get about that. The link --

DR. GUTMANN: Have we gotten all the trial-based data from agencies? Taking Defense off the table for a moment.

DR. SUGARMAN: Not all. Most. Most for fiscal year 2010. So we're starting with fiscal year 2010, basically as a way to test how well the system is working. We think it will work. And so the question -- we are beginning to get that information in. We can give you a detail of that, if it's --

DR. GUTMANN: Now, when you say "most," 95 percent? I mean what percent, approximately, have we gotten in?

MS. GROMAN: So out of the 18 we have asked,

taking DoD off of the table, we have gotten data from some or all data from -- for fiscal year 2010 -- from the other 17. So --

DR. GUTMANN: Including NIH?

MS. GROMAN: Including NIH. So --

DR. GUTMANN: Which is a huge part of --

MS. GROMAN: It is.

DR. GUTMANN: Yeah.

DR. SUGARMAN: So we will have that information. We'll see how well that performs.

The next step, if we do make the decision -- it sounds like there is a move to doing this next step -- we are now going to be exploring some new methodologic territory of linking the database, which is another test, with clinicaltrials.gov.

But if there is a move to go forward, I think it would be a rich experience. We don't know what it is going to yield, like many empirical studies. We don't know the answer going into it. But it seems worthwhile, given that we will have the most comprehensive database available, and comparing that to clinicaltrials.gov would promise to be a good use of

those -- that resource.

But I would respond to -- so Christine is right, the other projects are meant -- were suggested, in a way, to inform the second part of the commission's charge about how well things are working, requires different perspectives on that same picture. And so, if the commission wanted those data, then starting those might make sense, because they're not linked to the research project database. But it's really -- it's completely agnostic about that, from the perspective of the empirical advisory group or staff.

DR. WAGNER: Well, this was an enormous undertaking, and has the potential to be a great contribution. Everybody is looking for this kind of thing. So thank you both for your work. And I think, with that, we stand adjourned for a lunch break.

Again, Michelle, Jeremy, thank you so much.

DR. GUTMANN: Thank you very much.